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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,296	03/22/2004	Jaime A. Rabi	IDX1012C	1836

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KING & SPALDING LLP
1180 PEACHTREE STREET
ATLANTA, GA 30309-3521

EXAMINER

KRISHNAN, GANAPATHY

ART UNIT	PAPER NUMBER
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1623

MAIL DATE	DELIVERY MODE
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12/28/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/806,296

Applicant(s)

RABI, JAIME A.

Examiner

Ganapathy Krishnan

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-20, 69-81 and 83-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-20, 69-81 and 83-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 11/26/2007 has been entered.

The Request for Continued Examination filed 11/26/2007 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1-12, 21-68 and 82 have been canceled.
2. Claims 13, 17 and 83 have been amended.
3. Remarks drawn to rejections under 35 USC 112, first paragraph and 103.

Claims 13-20, 69-81 and 83-85 are pending in the case.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 13-20 and 69-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had full possession of the claimed invention, has been overcome by amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 13-20, 69-81 and 83-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gosselin et al (US 6,444,652, '652 patent) in combination with Weis et al (WO 96/13512), both of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Gosselin et al ('652) teaches the reaction of silylated uracil with a protected ribose sugar in dichloroethane to give the nucleoside 10, which is then deprotected (cols. 25-26, scheme at the bottom half of the page). The ribose sugar that is reacted with the silylated uracil is obtained from L-ribose by treatment of L-ribose with methanol and acid followed by protection of the hydroxyl groups with benzyl chloride in the presence of pyridine (base, acid scavenger; col. 19, Reaction 1). Hence, the reaction steps of forming 1-O-alkyl-ribose by reaction of a ribose with methanol and protection of the remaining free hydroxyl groups and its coupling to uracil via the

silylated derivative and subsequent deprotection of the protecting groups is taught by Gosselin. Even though the reactions above are performed with a ribose, one of ordinary skill in the art will recognize that the same reaction can be performed with a deoxyribose too. However, Gosselin et al do not teach the conversion of the 1-O-alkyl-ribose to a halide before reacting it with a silylated base.

Weis et al, drawn to preparation of ribofuranosyl nucleosides, teaches that the reaction of a silylated base with a ribose sugar that has a chlorine at the 1-position to give the corresponding nucleoside is performed using mild conditions and goes to completion in 2 hours (page 13, Scheme IV), whereas the same type of coupling with the ribose sugar having oxygenated leaving group (OAc in this case) takes 16 hours to go to completion (page 9, Scheme II). One of ordinary skill in the art will recognize from this teaching that having a halide at the 1-position speeds up the coupling step with the silylated base.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of the prior art as above in a process for the preparation of a beta-L-2'-deoxythymidine and beta-L-2'-deoxyuridine as instantly claimed, since the process steps and reagents for the desired products is seen to be taught in the prior art using the structurally close ribose sugar.

One of ordinary skill in the art would be motivated to use the process as instantly claimed since the process is mild and the step wherein the ribose containing the halide at the 1-position is coupled to the silylated base (as taught in Scheme IV, page 13 of Weis) is fast compared to the same step wherein the ribose has an oxygenated leaving group. A reaction step that is art tested to be fast and yields the desired product in high yield is preferable. The skill artisan also knows

that the reaction sequence performed with a ribose will also work equally well with a deoxy ribose.

It is well within the purview of one of ordinary skill in the art to adjust process parameters, ratios of reagents and substitute different solvent(s), reagents, etc., in order to optimize the yield of the desired product. The use of milder acids instead of the strong sulfuric acid is also an obvious variant since both are sources of H^+ needed as a catalyst and a mild acid is preferable.

Response to Applicants Arguments

Applicants' have traversed the rejection arguing that:

1. Gosselin in reaction 1 at col. 19 does not teach the conversion of 1-O-alkylribose to a halide before reacting it with a silylated base because none of the reaction intermediates 141, 142 and product 143 is a halide. And he does not teach or suggest an anhydrous acid halide produced by the reaction of an acyl halide with an alcohol, much less being produced in situ.

2. Weis, at page 20 merely discloses that structure 55 is converted to structure 56 by added HCl. He does not teach or disclose that the acid halide can be produced by the reaction of an acyl halide with an alcohol much less it is produced in situ.

In view of the above the instant invention is not rendered obvious according to the applicants. Applicants' arguments are not found to be persuasive.

Gosslein et al ('652) teaches the reaction of silylated uracil with a protected ribose sugar in dichloroethane to give the nucleoside 10, which is then deprotected (cols. 25-26, scheme at the bottom half of the page). The ribose sugar, (structure 1, above the arrow) that is reacted with the

silylated uracil is obtained from L-ribose by treatment of L-ribose with methanol and acid followed by protection of the hydroxyl groups with benzyl chloride in the presence of pyridine (base, acid scavenger; col. 19, Reaction 1). Hence, the reaction steps of forming 1-O-alkyl-ribose by reaction of a ribose with methanol and protection of the remaining free hydroxyl groups and its coupling to uracil via the silylated derivative and subsequent deprotection of the protecting groups, steps as instantly claimed, is taught by Gosselin. In Gosselin's process a 1-acetylated ribose is coupled to the silylated base (uracil). This is similar to the instant process step even though Gosselin does not use a 1-halodeoxyribose. But one of skill in the art would recognize that the same process step can be used with a deoxyribose too.

Weis et al, drawn to preparation of ribofuranosyl nucleosides, teaches the reaction of a silylated base with a ribose sugar that has a chlorine at the 1-position to give the corresponding nucleoside is performed using mild conditions and goes to completion in 2 hours (page 13, Scheme IV), whereas the same type of coupling with the ribose sugar having oxygenated leaving group (OAc in this case) takes 16 hours to go to completion (page 9, Scheme II). One of ordinary skill in the art will recognize from this teaching that having a halide at the 1-position of the ribose ring (as instantly claimed) speeds up the coupling step with the silylated base.

Whether an acid halide is generated in situ or not, the end product is the same. At page 20, Weis teaches the conversion of structure 55 (protected deoxyribose) to the 1-halo derivative (structure 56). Structure 55 is produced from structure 54 via reactions as instantly claimed (as seen in Figure 3). Even though the halodeoxyribose in the reaction scheme of Weis is formed by reacting with added HCl it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute HCl with another source of halogen like an acyl halide in a

process for the preparation of the 1-halo-2-deoxyribose and beta-L-2'-deoxythymidine and beta-L-2'-deoxyuridine as instantly claimed, since the process steps and reagents for making the desired product is seen to be taught in the prior art using a structurally close ribose sugar and analogous reagents. Irrespective of whether an acid halide is generated in situ or not the end result is the formation of the halosugar.

One of ordinary skill in the art would be motivated to use the process as instantly claimed since the process is mild and step wherein the ribose containing the halide at the 1-position is coupled to the silylated base is fast compared to the same step wherein the ribose has an oxygenated leaving group. A reaction step that is art tested to be fast and yields the desired product in high yield is preferable. The skilled artisan also knows that the reaction sequence performed with a ribose will also work equally well with a deoxy ribose. One of skill in the art would also be motivated to substitute HCl with other sources of halogen like acyl halides for the halogenation step in order to optimize yields of the halosugar.

Conclusion

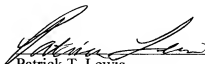
Claims 13-20, 69-81 and 83-85 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK



Patrick T. Lewis
Primary Patent Examiner
Art Unit 1623